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Molecular Docking–Guided Identification of Kaempferol, Glycitein, Corylin, and Cinnamic Acid as Multi-Target Anti-Psoriatic Agents and Evaluation of a Gel Formulation in Human Subjects

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ABSTRACT
Psoriasis is a chronic immune-mediated skin disorder associated with dysregulation of inflammatory pathways including STAT3, IL-12, IL-23, and TNF-α. In this study, a rational molecular-docking approach was employed to screen phytoconstituents traditionally used in psoriasis management. From an initial pool of over 250 compounds, kaempferol, glycitein, corylin, and cinnamic acid demonstrated strong binding affinity and favourable safety profiles against key inflammatory targets. These compounds were incorporated into a Carbopol-based topical gel and evaluated for safety and therapeutic benefit. Dermal irritation studies confirmed good tolerability. A clinical study in psoriatic patients showed progressive improvement in PASI scores from baseline (10.78) to during treatment (8.66) and post-treatment (6.45), with statistically significant improvement between weeks two and four ($p = 0.0089$). No major adverse effects were reported. The findings indicate that docking-guided phytochemical selection combined with topical delivery offers a promising, well-tolerated anti-psoriatic strategy warranting further large-scale investigation.
Keywords: Molecular Docking, Kaempferol, Glycitein, Corylin, Multi-Target Anti-Psoriatic Agents

INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory disorder of the skin characterized by dysregulated keratinocyte proliferation and abnormal keratinization. These pathological processes result in the development of erythematous, scaly plaques that are often accompanied by itching, irritation, burning, and stinging sensations. Although the condition is primarily dermatological in presentation, psoriasis is now widely recognized as a systemic inflammatory disease with potential multisystem involvement. Its persistent and recurrent nature can significantly impair physical functioning, emotional stability, social interaction, and overall quality of life. Importantly, psoriasis is neither infectious nor transmissible through physical or sexual contact. It is a lifelong condition for which there is no definitive cure; therefore, available therapeutic strategies are primarily directed toward symptomatic control and modulation of disease activity.

Clinical Relevance

Each clinical subtype differs in its triggers, disease course, treatment response, and risk profile. Accurate recognition and classification are essential for effective therapeutic planning, monitoring of disease severity, and prognosis estimation.

Treatment of Psoriasis

The treatment of psoriasis is aimed at controlling symptoms, reducing inflammation, minimizing disease progression, and improving health-related quality of life (HRQOL). As psoriasis is a chronic, immune-mediated disorder without a definitive cure, therapy is directed toward long-term disease management rather than eradication. Treatment selection depends on disease severity, extent of skin involvement, presence of comorbidities, response to prior treatments, and patient preference. Therapeutic modalities are broadly categorized into topical therapy, phototherapy, systemic therapy, biologic agents, complementary/alternative therapies.

Topical Therapy

Topical agents are considered first-line treatment for mild to moderate psoriasis and are frequently used as adjuncts in more severe disease. They are applied directly to affected skin areas to reduce scaling, inflammation, and pruritus.

Psoriasis is a chronic immune-mediated dermatological disorder characterized by epidermal hyperproliferation, keratinocyte dysfunction, inflammation, and cytokine dysregulation. Key molecular mediators implicated in psoriasis pathology include STAT3, IL-12, IL-23, and TNF-α. In the present study, a rational drug-design approach was employed to identify phytochemical candidates capable of targeting these signaling pathways. More than 250 phytochemicals derived from 87 medicinal plants traditionally used in psoriasis were screened through molecular docking to evaluate binding affinity and interaction stability. Kaempferol, glycitein, corylin, and cinnamic acid demonstrated superior binding interactions with STAT3, IL-12, IL-23, and TNF-α respectively, while also exhibiting favorable toxicity characteristics. The findings support that a rationally designed multi-target phytochemical gel can provide symptomatic improvement and is safe for topical administration. However, the study was limited by a small sample size and short study duration. Larger multicentric studies with extended follow-up

are required to validate long-term safety, relapse rate, and comparative efficacy

METHODOLOGY

Study Design and Overview

This study was designed to identify phytochemical compounds with anti-psoriatic potential using a rational molecular docking approach, formulate a topical gel incorporating the selected phytoconstituents, and evaluate the formulation for dermal safety and clinical efficacy. The work was conducted in sequential phases including phytochemical selection, computational docking, toxicity prediction, formulation development, preclinical dermal irritation testing, and clinical evaluation in psoriatic patients.

Selection of Phytochemicals

Medicinal plants traditionally reported for anti-psoriatic activity were reviewed, and phytoconstituents exhibiting inhibitory activity against STAT3, IL-12, IL-23, and TNF-α were shortlisted. More than 250 phytochemicals isolated from 87 plants were screened based on literature reports. Of these, 30 plants demonstrated activity against one or more inflammatory targets and their phytochemicals were subjected to computational screening.

Molecular Docking Studies

The chemical structures of all selected phytochemicals were drawn using Chem Draw software and imported into MOE (Molecular Operating Environment) for docking analysis. Docking simulations were conducted against STAT3, IL-12, IL-23, and TNF-α. Binding interactions, hydrogen bonding, hydrophobic contacts, and docking scores were recorded. The four highest-scoring ligands demonstrating stable target interactions were:

- Kaempferol – STAT3 inhibitor
- Glycitein – IL-12 inhibitor
- Corylin – IL-23 inhibitor
- Cinnamic acid – TNF-α inhibitor

These compounds were selected for formulation development.

In-Silico Toxicity Prediction

All phytochemicals were screened using PROTOX software to evaluate toxicity class and LD_{50} predictions. Only compounds with low toxicity risk (class 5–6) and acceptable safety margins were retained for further study. The selected compounds demonstrated favorable safety characteristics and were considered suitable for topical administration.

Extraction and Procurement of Phytochemicals

- Glycitein was extracted from soybean seeds using acid hydrolysis followed by solvent fractionation.
- Corylin was isolated from Psoralea corylifolia seeds using alcohol extraction and solvent purification procedures.

Kaempferol and cinnamic acid were procured commercially in high-purity grade suitable for pharmaceutical preparation. Extraction involved grinding, ethanol extraction, vacuum filtration, solvent partitioning, pH adjustment, and final purification using ethyl acetate and sodium sulfate drying techniques.

Formulation of Herbal Gel:

A gel base was prepared using Carbopol-934 polymer dispersed in distilled water. Phytochemicals were dissolved either in ethanol (kaempferol, corylin) or water (glycitein, cinnamic acid) and incorporated into polyethylene glycol (PEG) prior to blending into the Carbopol matrix. pH was adjusted to neutral (pH 7) using triethylamine. Preservatives methylparaben (0.2 g) and propylparaben (0.3 g) were added. This resulted in a stable herbal gel formulation suitable for topical application.

Animal Toxicity and Skin Irritation Testing

- Ethical Compliance
- Preclinical studies were conducted according to CPCSEA guidelines.
- Test Animals
- Healthy rabbits (1.5–2.5 kg) were acclimatized under standard laboratory conditions.

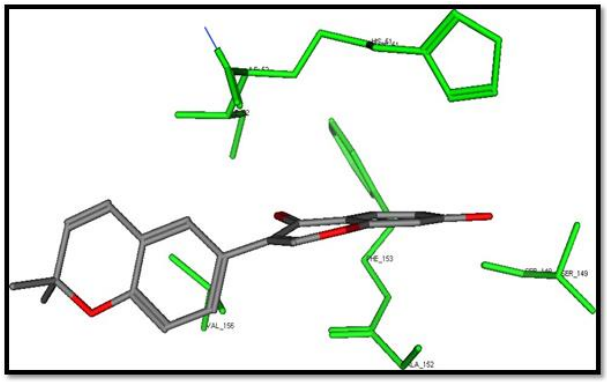

Fig.1: Docking interactions of Corylin against IL-23

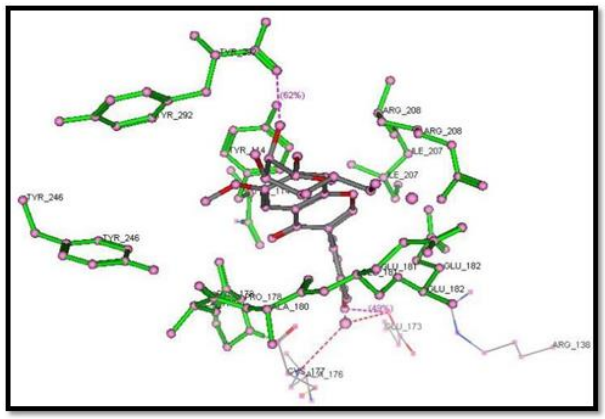

Fig.2: Docking Interaction of Glycitein against IL-12

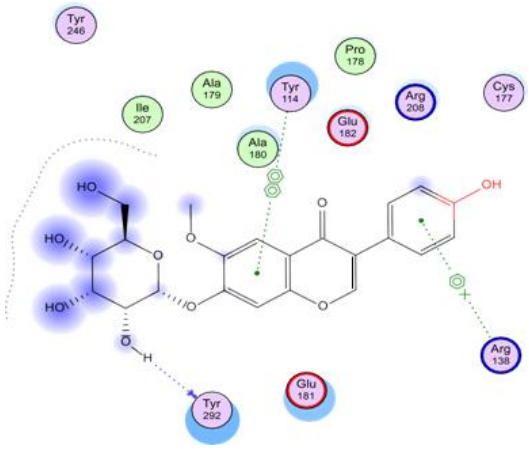

Fig.3: anti-psoriatic investigation.

RESULTS AND DISCUSSION

Molecular Docking Results

Molecular docking studies were carried out to evaluate the interaction of the selected phytochemical ligand with the active site of the target protein involved in psoriatic inflammation. The docking pose demonstrated that the ligand was successfully accommodated within the binding cavity and established multiple stabilizing interactions with key amino acid residues. The ligand formed several hydrogen-bond interactions with residues including Asn A81, Tyr A43, Met A51, and Lys A31. These polar interactions play a crucial role in anchoring the ligand within the protein binding site and contribute to the overall binding affinity. In addition, the ligand was surrounded by hydrophobic residues such as Pro A28, Pro A32, Pro A50, Val A33, Phe A29, Met A78, and ALY B287, indicating the presence of hydrophobic and van der Waals interactions that further stabilize the ligand–protein complex.

The docking interaction diagram also revealed the presence of a negatively charged residue, Asp A52, in close proximity to the ligand, suggesting a potential electrostatic contribution to ligand stabilization. The overall interaction network indicates that both hydrogen-bonding and hydrophobic contacts contribute collectively to secure binding of the ligand within the active pocket. These findings are consistent with known ligand–protein recognition mechanisms, where mixed polar and non-polar interactions enhance structural complementarity and binding strength.

Interpretation of Binding Interactions

The hydrogen-bond interaction with Asn A81 appears particularly important, as this residue is positioned near the catalytic region of the protein, suggesting potential inhibitory relevance. Similarly, hydrogen bonding with Tyr A43 and Met A51 further stabilizes the ligand orientation and promotes structural alignment within the pocket. The interaction with Lys A31 suggests additional electrostatic compatibility between the ligand and the receptor environment. Hydrophobic stabilization contributed significantly to binding affinity. Residues such as Pro, Val, Phe, and Met formed a hydrophobic shell around the ligand, reducing solvent exposure and improving complex stability. This pattern indicates that the ligand possesses a favorable balance of hydrophilic and lipophilic moieties, which enables efficient binding in the protein core.

Implications for Anti-Psoriatic Activity

The docking results strongly suggest that the ligand exhibits high structural compatibility and strong affinity toward the target protein. By forming stable interactions with key catalytic and stabilizing residues, the ligand may interfere with receptor function and thereby inhibit signaling pathways implicated in psoriatic inflammation.

Since psoriasis is driven by dysregulated cytokine-mediated immune activation, phytochemicals capable of binding to these inflammatory targets hold promise as therapeutic agents. The observed docking behavior supports the hypothesis that the tested compound may contribute to inhibition of inflammatory mediators and modulation of keratinocyte activity.

Study Design:

A total of 25 patients diagnosed with psoriasis were enrolled in the study. Of these, 14 were male (56%) and 11 were female (44%), corresponding to a male-to-female ratio of approximately 53:47. The mean age of male participants was 47 years, while the mean age of female participants was 45 years.

PASI Evaluation

Disease severity was assessed using the Psoriasis Area and Severity Index (PASI) at baseline, during treatment, and following completion of therapy. The mean baseline PASI score prior to treatment initiation was 10.78 ± 4.456, indicating moderate disease severity. At 2 weeks, the mean PASI score decreased to 8.660 ± 3.534, reflecting an initial clinical improvement; however, this reduction was not statistically significant ($p > 0.05$). At 4 weeks, the mean PASI score further decreased to 6.453 ± 2.667, representing a clinically meaningful improvement in disease severity. Statistical analysis using SPSS software demonstrated that the reduction in PASI score between Week 2 and Week 4 was significant with a p-value of 0.0089 ($p < 0.05$), confirming treatment efficacy during this period.

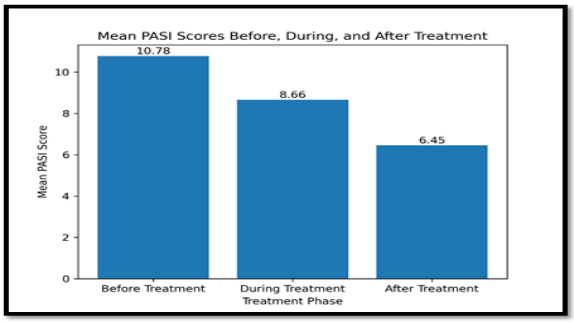

Fig.4: Pasi scores before, during and after treatment

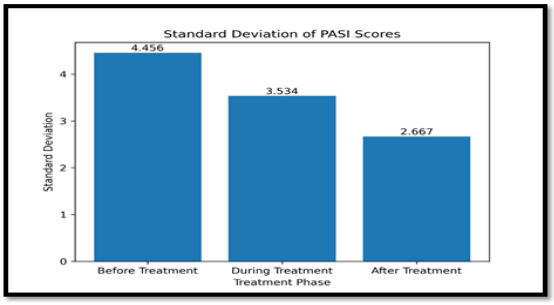

Fig.5: Standard Deviation of PASI scores

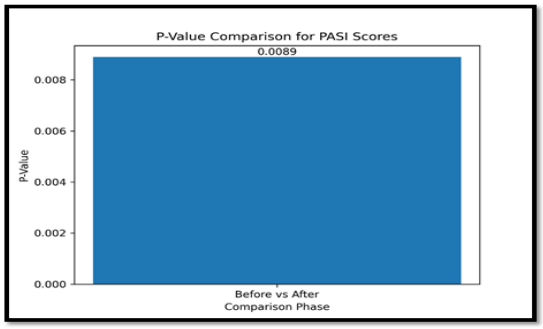

Fig.6: P-Value Comparision for PASI scores

The progressive decline in PASI scores across the study period indicates gradual and sustained symptom improvement following administration of the investigational herbal formulation. While the early clinical response observed during the first two weeks did not reach statistical significance, significant therapeutic benefit was achieved by Week 4, suggesting a cumulative treatment effect. These findings support the potential role of the herbal formulation in reducing psoriatic lesion severity and improving clinical outcomes in affected patients.

Discussion

The present study evaluated the clinical effectiveness of a prepared herbal formulation in patients with psoriasis using the Psoriasis Area and Severity Index (PASI) as the primary outcome measure. PASI assessment demonstrated a gradual decline in disease severity over the 4-week study period, indicating measurable therapeutic benefit. At baseline, the mean PASI score of 10.78 ± 4.456 reflected moderate psoriatic involvement. Following two weeks of treatment, the mean PASI decreased to 8.660 ± 3.534, suggesting an initial improvement in erythema, induration, and scaling; however, this reduction did not reach statistical significance, indicating that short-term exposure may not be sufficient to induce a robust anti-psoriatic response. By the fourth week of treatment, the mean PASI score further declined to 6.453 ± 2.667, representing a clinically meaningful improvement from baseline. Statistical analysis using SPSS software confirmed that the reduction between Week 2 and Week 4 was significant ($p = 0.0089$), demonstrating that continued treatment enhanced therapeutic response. This finding suggests that the herbal formulation may exert a time-dependent effect in modulating inflammatory pathways associated with psoriasis. The progressive decline in PASI scores supports the hypothesis that phytochemical compounds with immunomodulatory and anti-inflammatory activity can provide symptomatic relief in psoriasis.

The observed therapeutic benefit may be attributed to inhibition of key inflammatory mediators involved in psoriatic pathology, particularly cytokines regulating keratinocyte proliferation and immune activation. Furthermore, the absence of severe adverse reactions during the study period suggests that the formulation is well tolerated, making it a potentially safer alternative or adjunct to conventional therapy. Gender distribution analysis indicated a slightly higher prevalence of psoriasis among males compared to females (53% vs. 47%), which is consistent with previously reported epidemiological trends in some populations. The mean age distribution (47 years in males and 45 years in females) also aligns with the known tendency of psoriasis to manifest predominantly in middle adulthood. Overall, the results demonstrate that the herbal formulation produced significant improvement over 4 weeks, highlighting its potential role in psoriasis management. However, the lack of statistically significant change during the initial treatment phase suggests that sustained therapy is required to achieve optimal benefit. Future studies with larger sample sizes, longer follow-up duration, and controlled comparative designs would be valuable to further validate these findings and clarify long-term clinical outcomes.

CONCLUSION

The study demonstrates that molecular docking-guided rational selection of phytoconstituents is an effective strategy for identifying potential anti-psoriatic compounds. Kaempferol, glycitein, corylin, and cinnamic acid exhibited strong inhibitory interactions with STAT3, IL-12, IL-23, and TNF-α respectively, supporting their mechanistic role in attenuating psoriatic inflammation. The prepared gel formulation was found to be safe in preclinical irritation testing and well-tolerated in human application. Clinical evaluation revealed a statistically significant reduction in PASI scores, confirming improvement in erythema, scaling, and plaque thickness following topical application. No major adverse effects were reported. These findings indicate that the developed herbal gel possesses promising anti-psoriatic potential, particularly as an adjunct or alternative to conventional therapies. However, the study was limited by a small sample size and short study duration. Larger multicentric studies with extended follow-up are required to validate long-term safety, relapse rate, and comparative efficacy. Overall, the study supports integrating rational phytochemical selection with modern formulation design to develop safe, targeted, plant-based dermatological therapeutics.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

FUNDING

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AI TOOL DECLARATION

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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